

From the INTERNATIONAL BUREAU

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NOTIFICATION CONCERNING
TRANSMITTAL OF COPY OF INTERNATIONAL
PRELIMINARY REPORT ON PATENTABILITY
(CHAPTER I OF THE PATENT COOPERATION
TREATY)

(PCT Rule 44bis, 1(c))

To:

HAMMANN, Heinz
Binger Str. 173
55216 Ingelheim Am Rhein
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Eingang Patents Germany

Date of mailing (day/month/year)
17 March 2011 (17.03.2011)

21. März 2011

Applicant's or agent's file reference
P01-2439/WO1

SdT/No: Yes:

SB gesehen erledigt

IMPORTANT NOTICE

International application No.
PCT/EP2009/061455International filing date (day/month/year)
04 September 2009 (04.09.2009)Priority date (day/month/year)
08 September 2008 (08.09.2008)

Applicant

BOEHRINGER INGELHEIM INTERNATIONAL GMBH et al

The International Bureau transmits herewith a copy of the international preliminary report on patentability (Chapter I of the Patent Cooperation Treaty)

The International Bureau of WIPO
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference P01-2439/WO1	FOR FURTHER ACTION	See item 4 below
International application No. PCT/EP2009/061455	International filing date (day/month/year) 04 September 2009 (04.09.2009)	Priority date (day/month/year) 08 September 2008 (08.09.2008)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant BOEHRINGER INGELHEIM INTERNATIONAL GMBH		

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).																								
2.	This REPORT consists of a total of 7 sheets, including this cover sheet. In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.																								
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%;"> <tr> <td style="width: 5%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 25%;">Box No. I</td> <td style="width: 70%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input checked="" type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<input checked="" type="checkbox"/>	Box No. VIII	Certain observations on the international application																							
4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																								

<p style="text-align: center;">The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 338 82 70</p>	<p>Date of issuance of this report 08 March 2011 (08.03.2011)</p> <hr/> <p>Authorized officer Agnes Wittmann-Regis</p> <p>e-mail: pt06.pct@wipo.int</p>
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PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below

International application No.
PCT/EP2009/061455

International filing date (day/month/year)
04.09.2009

Priority date (day/month/year)
08.09.2008

International Patent Classification (IPC) or both national classification and IPC
INV. C07D487/04 A61K31/519 A61P25/00 A61P3/00

Applicant
BOEHRINGER INGELHEIM INTERNATIONAL GMBH

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office
Gitschiner Str. 103
D-10958 Berlin
Tel. +49 30 25901 - 0
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Date of completion of
this opinion

see form
PCT/ISA/210

Authorized Officer

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**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2009/061455

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. ☐ This opinion has been established taking into account the **rectification of an obvious mistake** authorized by or notified to this Authority under Rule 91 (Rule 43bis.1(a))
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
4. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
5. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/EP2009/061455

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	<u>1-29</u>
	No: Claims	
Inventive step (IS)	Yes: Claims	
	No: Claims	<u>1-29</u>
Industrial applicability (IA)	Yes: Claims	<u>1-29</u>
	No: Claims	

2. Citations and explanations

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/EP2009/061455

Re Item V.

Reference is made to the following documents:

- D1 : WO 2004/026876 A (BAYER HEALTHCARE AG [DE]; HENDRIX MARTIN [DE]; BOESS FRANK-GERHARD [DE] 1 April 2004 (2004-04-01) cited in the application
- D2 : WO 2004/018474 A (BAYER HEALTHCARE AG [DE]; HENDRIX MARTIN [DE]; BOESS FRANK-GERHARD [DE] 4 March 2004 (2004-03-04) cited in the application
- D3 : WO 2004/096811 A (PFIZER PROD INC [US]; BELL ANDREW SIMON [GB]; DENINNO MICHAEL PAUL [US] 11 November 2004 (2004-11-11)

1 Claim 28 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 39.1(iv) / 67.1(iv) PCT.

The patentability can be dependent upon the formulation of the claims. The EPO, for example, does not recognise as patentable claims to the use of a compound in medical treatment, but may allow claims to a product, in particular substances or compositions for use in a first or further medical treatment.

2 Novelty

The present application meets the requirements of Article 33(2) PCT because the subject-matter of claims 1-29 is considered to be new over the prior art D1 to D3 for the following reasons:

Documents D1-D2 refer to structurally very close pyrazolo(3,4-d)pyrimidine compounds also useful for the treatment of central nervous system disorders (CNS), which only differ in that the cycloalkyl moiety A in position 1 is not substituted (see D1, especially examples 1A, 2A, 4A, 5A, 1, 2, 4-6, 15, 17, 18, 20, 23 and claims; D2, examples 1A, 2A, 4A, 5A, 1-6, 8, 12-14 and claims).

Document D3 describes structurally very close pyrazolo(3,4-d)pyrimidine compounds (see especially examples 4, 14, 15, 17, 43 and claims 1 to 8) also useful for the treatment of diseases like diabetes, obesity hyperglycemia, dyslipidemia, etc.. which only differ in that the cycloalkyl moiety A in position 1 is not substituted.

3 Inventive step

3.1 Closest State of the Art and Difference

D1-D3 are considered to represent equally the closest prior art, since these documents disclose structurally very close phosphodiesterase 9A inhibitors (PDE9A) useful in treating CNS as well as diseases like diabetes, obesity hyperglycemia, dyslipidemia, etc..

It should be noted that the mode of action of compounds is an intrinsic property of the compounds and cannot be a base for an inventive step acknowledgement. Moreover the discover of a new mechanism of action cannot make a known use of a known compound novel and also inventive.

The compounds of present claim 1 differ only in that the cycloalkyl moiety A is unsubstituted.

3.2 Technical Effect and Problem

The application as filed does not contain any evidence that this distinguishing feature is responsible for an unexpected effect.

Consequently, the problem underlying the present application should be seen in providing a substitution on a cycloalkyl moiety of a already known structure in order to obtain compounds useful in treating CNS disorders as well as diseases like diabetes, obesity hyperglycemia, dyslipidemia, etc..

In view of the examples and the biological data of pages 75-77 of the present application it is credible that this problem has actually been solved by the subject-matter of claim 1.

3.3 Obviousness of the solution

For a skilled worker, looking for further compounds, the replacement of a hydrogen atom by a substituent is a routine measure which belongs to the common practice in the field of medicinal chemistry; thus being confirmed by the Applicant himself in claim

1 by the definition of x being 0 to 4; R⁴, R⁵ as well as using expressions like "with the above mentioned members may optionally be substituted". Substitutions of the structurally very close compounds of D1-D2 have also been considered by the skilled person (see claim 1 respectively).

Thus claims 1 to 29 do not meet the requirements of Art. 33(3) PCT.

Re Item VIII.

There is a discrepancy between claim 1 and dependent claim 19 due to the presence of a proviso in the dependent claim 19, which is missing in the main claim.

The use of the expressions "preferably" or "more preferably" in claims 1, 3, 7, 13 to 17 and 26 renders the subject-matter of those claims unclear since these expressions introduce an ambiguity in the claims. It is stressed that these expressions have no limiting effect on the scope of the claims. Furthermore these claims are thus not concise.